

ABSTRACT

Methods of designing protein-targeted peptides or peptide analogues whose sequences are derived from the target protein sequences, using target protein sequence, analytically derived templates, and relevant distributions of amino acids for weighted random assignments to those templates. The templates are derived from eigenvectors of the autocovariance matrices of the physicochemically-transformed amino acid sequence of the target proteins; wavelet subsequence templates derived from wavelet transformations of the physicochemically-transformed amino acid sequence of the target proteins; and/or non-overlapping redundant subsequence templates computed from the physicochemically-transformed target protein amino acid sequence. The protein targets include cell receptors; transporters; enzymes; chaperonins; antibodies; surface proteins of infectious agents; and any protein involved in protein-protein interactions. The peptides are designed to bind to and/or otherwise modulate the function of the target protein. Partitioned amino acid distributions for weighted random assignments to the similarly partitioned templates are derived from a variety of physiologically relevant amino acid pools or regions in the target protein sequence relevant to the construction of the templates. Sequential pattern ("mode") matches between candidate peptides and their target proteins are designed such that when examined by maximum entropy, all poles power spectral transformations and/or wavelet transformations, they yield peaks of wavenumbers that differ by  $\leq 10\%$  of the larger wavenumber value. Also provided are examples of such mode-matched peptides, as well as methods for their use in elucidating sites on proteins for drug design and testing, detection of disease conditions or contaminants, and as therapeutics for protein function modulation in disease treatment.

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